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Division of Dockets Management (HFA –305)
Food and Drug Administration
5630 Fishers Lane - Room 1061
Rockville, MD 20852

VIA FACSIMILE (301) 827-6870

RE: Federal Measures To Mitigate BSE Risks: Consideration for Further Action *[Docket 2004N-0264]*

Dear Sir or Madam:

Abbott Laboratories submits the following comments regarding the FDA Advanced Notice of Proposed Rulemaking, "Federal Measures To Mitigate BSE Risks: Consideration for Further Action," published in the Federal Register on July 14, 2004 at 69 FR 42288.

A wide range of critical medical technologies, such as *in vitro* diagnostic devices (IVDs) used for disease diagnosis and screening of the nation's blood supply, incorporate bovine-derived components. Abbott is committed to assuring the continued safety of its products and will continue its cooperation with FDA and the USDA in this regard. Further, we support the efforts of FDA and USDA to assure the safety of the human food and animal feed chains.

As FDA and USDA consider measures to continue to assure the safety of the human food and animal feed chains, potential implications to the manufacture of medical technologies, such as IVDs, must not be overlooked. Bovine-derived components, such as blood and enzymes from the small intestine, serve critical functions in many medical technologies.

It is difficult to predict with certainty the impact to the medical device industry of proposals designed to assure the safety of the human food and animal feed chains. However, in our past experience measures taken to assure the safety of the human food and animal feed chains, such as general import bans of bovine-derived materials, have

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had a seriously negative, albeit unintentional, impact on our ability to produce medical products. Rules designed to protect the human food and animal feed chains, must be designed in such a way as to allow the medical technology industry access to the components necessary to manufacture medical devices, such as IVDs, which do not have human nor animal contact. General prohibitions on the use of or the ability to obtain bovine-derived materials have a crippling affect on our industry. Rather than prohibitions on material use or a requirement for denaturing of material, allowing appropriate labeling of the materials must be the method of choice. Examples of appropriate labeling are "intended for medical manufacture" and "not for use in human or animal food."

While many of the 36 questions posed by FDA and USDA do not have a direct bearing on our medical device products, several of the questions have the potential to impact our ability to manufacture IVDs. It is to these questions, we provide comment. The identified number of each question below reflects the corresponding number in the advanced notice of proposed rulemaking.

2. What data or scientific information is available to evaluate the IRT recommendation described above, including that aspect of the recommendation concerning what portion of the intestine should be removed to prevent potentially infective material from entering the human food and animal feed chains?

While we support measures deemed necessary by FSIS and FDA to ensure safe human and animal food chains, the agencies must implement such measures in a manner that does not impact other industries that rely on by-products of the small intestine. Specifically, enzymes derived from the small intestine are an essential component of many *in vitro* diagnostic devices (IVDs) intended for human use, which have no patient, user, or animal contact. Any decision to remove the small intestine must not adversely impact the ability of IVD manufacturers to obtain, transport, import/export, or use by-products of the small intestine in the manufacturer of medical products.

In our experience, measures taken to assure human food and animal feed chain safety have had a seriously negative, albeit unintentional, impact on our ability to source manufacturing materials for life-saving IVDs. Import bans have severely impacted our ability to source manufacturing materials. The negative impact to our industry of requiring the removal of the entire small intestine from the human food and animal feed chains must be considered. Provisions allowing continued use of this material for non-food purposes must be implemented in a manner that does not place undue burden on the IVD industry. Requirements to denature material, such as the small intestine, would render it useless for the manufacturer of the IVD for which it is a critical component.

Further, efforts to ensure that the entire small intestine is not considered, designated, or referenced as specified risk material (SRM) is of utmost importance. The ability to attest that bovine-derived components are not sourced from SRMs is essential to global trade. Materials derived from other portions of the small intestine, such as the duodenum or jejunum must continue their status as non-SRM. We note FDA's interim final rule Use of Materials Derived From Cattle in Human Food and Cosmetics clearly articulates that the

reason for removal of the entire small intestine is to ensure effective removal of the distal ileum, rather than defining or specifying the small intestine as an SRM[1].

Maintaining the current status of the small intestine, with the exception of the distal ileum, as non-SRM is also supported by scientific evidence. The agent has been documented to be found in certain lympho-reticular system tissues called the Peyer's patches, which are concentrated in the distal ileum of the small intestine[2]. Current research indicates that the infective agent is not found in other gastro- intestinal tissues other than the distal ileum[3]. Specifically, research has shown that the infective agent is not present in the duodenum and the jejunum portions of the small intestine even when the agent is found in the ileum[4]. Additionally, the infective agent for BSE has only been found in the distal ileum of cattle, which were inoculated with the BSE infective agent; due to the increased amount of infective agent the animals were exposed to; the agent has not been reported to be found in animals, which have succumbed to the disease naturally[5].

6. If SRMs are prohibited from animal feed, what requirements (labeling, marking, denaturing) should be implemented to prevent cross-contamination between SRM-free rendered material and material rendered from SRMs?

The impact of these measures to other industries must be thoroughly considered as FDA implements requirements to prevent cross-contamination. As noted earlier, enzymes sourced from the small intestine are a vital component to IVDs. Any requirement to denature the entire small intestine would render it useless, thus destroying our ability to manufacture medically necessary IVDs. Rather than imposing prohibitions on material use or denaturing of material, appropriate labeling of materials, such as "intended for medical device manufacture" and "not for use in human or animal food," must be the method of choice.

15. Is there scientific evidence to show that the use of bovine blood or blood products in feed poses a risk of BSE transmission in cattle and other ruminants?

Bovine blood and blood products are a critical component of IVDs. Often used as protein stabilizers in IVD reagents and as an essential component of culture media for the production of antibodies. Decisions in regard to the use or handling of bovine blood and blood products must bear this in mind. Subjecting blood and blood products to treatment (e.g., heat) will destroy the material, rendering it useless. Banning blood and

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[1] 69 FR 42259 (July 14, 2004)

[2] Wells, G.A.H., Dawson, M., Hawkins, S.A.C., Green, R.B., Dexter, I., Francis, M. E., Simmons, M. M., Austin, A. R., Horigan, M. W., 1994: Infectivity in the ileum of cattle challenged orally with bovine spongiform encephalopathy. The Veterinary Record: 135, pages 40-41.

[3] Wells, G.A.H., Hawkins, S.A.C., Green, R.B., Austin, A. R., Dexter, I., Spencer, Y. I., Chaplin, M. J., Stack, M. J., Dawson, M., 1998: Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy (BSE): an update. The Veterinary Record; 142 pages 103-106

[4] Terry, L. A., Marsh, S., Ryder, S. J. Hawkins, S. A. C., Wells, G. A. H., Spencer, Y. II, 2003: Detection of disease specific PrP in the distal ileum of cattle exposed orally to the agent of bovine spongiform encephalopathy. The Veterinary Record: 152, pages 387-392.

[5] Wells et al., 1998; Terry et al., 2003

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blood products in animal feed must not unintentionally impact the ability of medical device manufacturers to obtain, use, transport, or import/export bovine blood and blood products intended for the manufacture of medical devices, including IVDs.

28. Should FDA include exemptions to any new requirements to take into account the future development of new technologies or test methods that would establish that feed does not present a risk of BSE to ruminants?

Yes, however international acceptance of such a broad exemption should be considered. Global trade would be hindered where an exemption does not receive national recognition.

Thank you for the opportunity to provide these comments. Should you have any questions, please contact me at (847) 937-8197 or by facsimile at (847) 938-4422.

Sincerely,

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